

Chapter 15: Acne Vulgaris

INTRODUCTION

- *Acne* is a chronic skin condition marked by comedones and inflammatory lesions such as papules, pustules, and nodules.

CLINICAL PRESENTATION

- *Noninflammatory acne* lesions include closed comedones (whiteheads) and open comedones (blackheads). Closed comedones are the first visible lesions in acne and often rupture. Open comedones form when the plug extends to the upper canal and dilates the opening.
- *Inflammatory* lesions include papules, pustules, and nodules. Pus forms as neutrophils are recruited into the follicle during inflammation and *Cutibacterium acnes* releases chemokines. *C. acnes* also produces enzymes that increase follicular wall permeability, leading to rupture and release of keratin, lipids, and irritating free fatty acids into the dermis.
- Lesions typically appear on the face, back, neck, shoulders, and chest and may extend to the buttocks or limbs. One or more areas may be affected; once established, the pattern usually remains constant. The skin, scalp, and hair are often oily.
- Lesions may take months to heal. Nodules and deep lesions can cause scarring. Inflammatory lesions may resolve with erythematous or pigmented macules (hyperpigmentation) that can persist for months or longer, especially in darker skin tones.

DIAGNOSIS

- Diagnosis is based on patient assessment, including lesion observation and exclusion of other potential causes (eg, drug-induced acne). Various systems are used to grade acne severity.

TREATMENT

- Goals of Treatment: Reduce lesion number and severity, improve appearance, slow progression, limit duration and recurrence, prevent scarring and hyperpigmentation, and minimize psychological impact.

GENERAL APPROACH

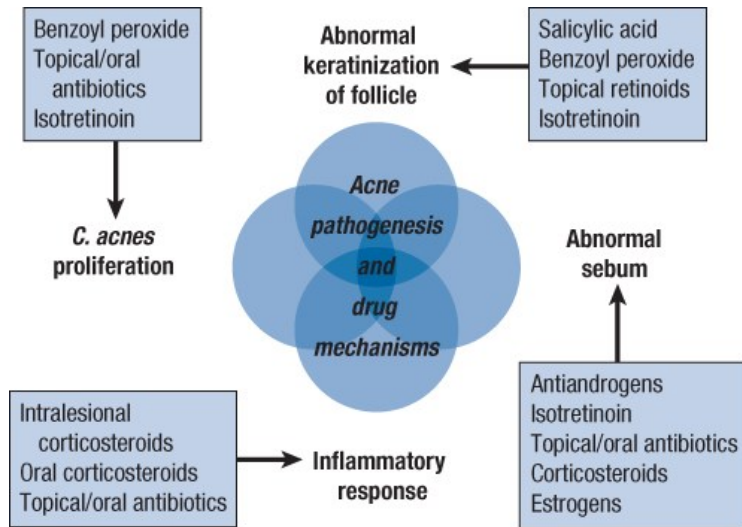
- Acne is a chronic disease that warrants early, aggressive treatment (**Fig. 15-1**). Maintenance therapy is often needed for optimal results. Adherence to long-term regimens is essential for sustained control.
- Eliminating follicular occlusion halts the acne cascade. Both nondrug and pharmacologic strategies should focus on cleansing, reducing triggers, and combination therapy targeting the four pathogenic mechanisms.
- Combination therapy is often more effective than single therapy and may reduce side effects, resistance, and tolerance to individual agents.
- Topical therapy is standard for mild-to-moderate acne, while systemic treatment is needed for moderate-to-severe cases.
- First-, second-, and third-line therapies should be selected and adjusted based on disease severity and stage. Treatment aims for control, not cure, with regimens tapered over time according to response.
- Use the fewest agents at the lowest effective doses to ensure efficacy, safety, resistance prevention, and adherence. Once control is achieved,



simplify the regimen but maintain suppressive therapy.

FIGURE 15-1

Acne pathogenesis and drug mechanisms.



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NONPHARMACOLOGIC THERAPY

- Encourage patients to avoid aggravating factors (eg, mechanical occlusion, cosmetics), follow a balanced low-glycemic-load diet, and manage stress.
- Patients should wash twice daily with a mild, nonfragranced opaque or [glycerin](#) soap or a soapless cleanser. Scrubbing should be minimized to prevent follicular rupture.
- Males using a safety razor should soften the beard with soap and warm water or shaving gel. Shaving should be light and infrequent, using a sharp blade and avoiding nicking lesions. Strokes should be in the direction of hair growth, shaving each area only once to limit irritation.
- Comedone extraction provides immediate cosmetic benefit but lacks extensive clinical trial support.
- Light therapies likely work by killing *C. acnes* and shrinking sebaceous glands to reduce sebum production, with few or temporary adverse effects. They may be used once or twice weekly for 6–10 treatments, with each lasting 10–20 minutes. Home-use blue light therapy is now available.

PHARMACOLOGIC THERAPY

- *Comedonal noninflammatory acne*: Use topical agents that reduce keratinization through exfoliation. Topical retinoids (especially [adapalene](#)) or fixed combinations with a retinoid (eg, [adapalene](#) + benzoyl peroxide) are preferred. Benzoyl peroxide, azelaic acid, and salicylic acid are second-line options.
- *Mild-to-moderate papulopustular inflammatory acne*: Reducing *C. acnes* in follicles is key. First-choice treatments include [adapalene](#) + benzoyl peroxide or individual agents such as benzoyl peroxide, topical retinoids, or azelaic acid. In moderate cases, fixed combinations are preferred, with or without hormonal therapy or antibiotics, especially if the trunk is affected. Alternatives include blue light monotherapy, other combinations (eg, [erythromycin](#) + [tretinoin](#)), or oral zinc. For widespread disease, consider oral antibiotics with topical benzoyl peroxide with or without [adapalene](#).

- *Moderately severe or severe papulopustular or moderate nodular acne:* Preferred treatment is an oral antibiotic plus a fixed-dose topical combination. Oral **isotretinoin** or hormonal therapy may also be used. If these are unsuitable, consider oral antiandrogens with oral antibiotics or topical therapy.
- *Nodular or conglobate acne:* Oral **isotretinoin** monotherapy is first-line. Alternatives include fixed-dose retinoid combinations or oral antibiotics. In females, oral **isotretinoin** plus antiandrogenic hormonal therapy is preferred. Alternatively, combine a fixed retinoid formulation with oral antibiotics and/or an oral antiandrogen.
- *Maintenance acne therapy:* A topical retinoid alone or with benzoyl peroxide (fixed dose) is most recommended. Azelaic acid is an alternative. Maintenance typically starts after 12 weeks of induction and continues for 3–4 months or longer to prevent relapse. Long-term antibiotic use is discouraged to reduce resistance.

Exfoliants (Peeling Agents)

- Exfoliants cause mild, continuous drying and peeling by irritating and damaging superficial skin layers, triggering inflammation. This stimulates mitosis, thickens the epidermis, and increases horny cells, scaling, and erythema. Reduced sweating creates a drier, less oily surface, which may help resolve pustular lesions.
- **Resorcinol** is less keratolytic than salicylic acid and is classified by the FDA as category II (not generally recognized as safe and effective) when used alone. However, 2% resorcinol and 3% resorcinol monoacetate are FDA-approved when combined with 3%–8% sulfur. Resorcinol is an irritant and sensitizer; it should not be applied to large areas or broken skin. It may cause a reversible dark brown scale in dark-skinned individuals.
- **Salicylic acid** is a comedolytic agent available over the counter (OTC) in 0.5%–2% strengths; 3%–6% concentrations are keratolytic, softening the horny layer and promoting scale shedding. It is mildly antibacterial and anti-inflammatory at concentrations up to 5%. Though FDA-approved, it offers no clear advantage over benzoyl peroxide or topical retinoids. Still, it is often used as first-line therapy for mild acne due to OTC availability in pads, washes, bars, and semisolids. Both wash-off and leave-on forms are well tolerated. Lower concentrations are sometimes combined with sulfur for additive effect. Prescription strengths of 5%–10% may be used, starting low and increasing with tolerance. It is often used when patients cannot tolerate topical retinoids because of irritation.
- **Sulfur** is keratolytic and antibacterial, helping resolve pustules and papules, masking lesions, and causing skin peeling through irritation. Used in 2%–10% concentrations, it is often combined with salicylic acid or resorcinol for greater effect, but use is limited by odor and more effective alternatives.

Topical Retinoids

- Retinoids reduce follicular obstruction and are effective for both comedonal and inflammatory acne. They reverse abnormal keratinocyte desquamation, act as keratolytics, and inhibit microcomedone formation, reducing mature comedones and inflammatory lesions.
- Topical retinoids are safe, effective, and economical for all but the most severe acne. They should be the first-line treatment for moderate acne—used alone or with antibiotics and benzoyl peroxide—then continued alone for maintenance. Combination products with benzoyl peroxide or topical antimicrobials are available.
- Retinoids may induce long remissions, though irritation can affect adherence. Side effects (dryness, peeling, erythema) can be minimized by reduced application frequency.
- Apply retinoids at night, 30 minutes after cleansing. Start with every other night for 1–2 weeks to adjust to irritation. Increase the dose only after 4–6 weeks of using the lowest concentration and least irritating vehicle. Gels and creams are less irritating than solutions.
- **Tretinoin** (retinoic acid, vitamin A acid) is available in multiple strengths and forms (creams, gels, pumps). It should not be used in pregnant women due to fetal risk.
- **Adapalene** (Differin) is as effective as and less irritating than other retinoids. It comes in a 0.1% OTC gel for once-daily use in patients age 12 years

and older), and also in cream, solution, lotion, and pads. A 0.3% gel and fixed-dose combinations with benzoyl peroxide are also available to enhance efficacy.

- **Tazarotene** (Tazorac) matches **adapalene**'s efficacy when used half as often. Compared to **tretinoin**, it is similarly effective for comedonal and more effective for inflammatory lesions when applied once daily. It is available as a 0.045% lotion and is not degraded by sunlight. **Tazarotene** is contraindicated in pregnancy.
- **Trifarotene** (Aklief) is FDA-approved for acne in patients aged 9 years and older. It comes as a 0.005% cream for once-daily evening use. Avoid during pregnancy.

Topical Antibacterial Agents

- **Benzoyl peroxide** is bactericidal to *C. acnes* and mildly comedolytic. It suppresses sebum and reduces comedogenic, inflammatory free fatty acids. Resistance has not been reported; combining it with antibiotics improves efficacy and may limit resistance.
 - ✓ Effective for both noninflammatory and inflammatory acne, benzoyl peroxide works quickly—reducing inflamed lesions within 5 days. It is a first-line agent, alone or with **adapalene**, for mild-to-moderate inflammatory acne and second-line for noninflammatory comedonal acne. Often combined with a topical retinoid or antibiotic, it can also be added to a retinoid for maintenance.
 - ✓ Available in topical washes, foams, creams, or gels (leave-on or wash-off), in strengths from 2.5% to 10%. All single-agent products are OTC.
 - ✓ Start with the lowest strength (2.5%) in a water-based formulation at night. If tolerated, increase to 5% or switch to acetone/**alcohol** gels or paste. The product should be washed off in the morning; apply sunscreen during the day.
 - ✓ Side effects include dryness, irritation, and rarely allergic contact dermatitis. It may bleach hair, clothes, and towels.
- **Topical clindamycin** and **erythromycin** are macrolide antibiotics effective and well-tolerated for acne. They are recommended in combination with topical benzoyl peroxide (wash-off or leave-on) or retinoids to boost efficacy and reduce resistance. **Clindamycin** is preferred due to better efficacy and no systemic absorption; it is available alone or with benzoyl peroxide. **Erythromycin** is available alone or with retinoic acid or benzoyl peroxide but is rarely used.
- A triple-combination gel—**clindamycin phosphate 1.2%, adapalene 0.15%, and benzoyl peroxide 3.1% (Cibtreo)**—is FDA-approved for acne in patients ≥12 years. Once-daily use led to treatment success (≥2-grade reduction and clear/almost clear skin at week 12) in 50% of study patients. Common side effects include burning, stinging, scaling, itching, and erythema; daily sunscreen is recommended.
- **Azelaic acid** has antibacterial, anti-inflammatory, and comedolytic activity. It is used for mild-to-moderate inflammatory acne but is less effective than other treatments. It serves as an alternative for comedonal and inflammatory acne, especially in combination, and as a maintenance option instead of topical retinoids. It is well tolerated; pruritus, burning, stinging, and tingling occur in 1%–5% of patients, while erythema, dryness, peeling, and irritation occur in fewer than 1%. Available as 20% cream (**Azelex**) and 15% gel (**Finacea**), it is typically applied twice daily to clean, dry skin. Most patients improve within 4 weeks, though treatment may continue for months if needed.
- **Dapsone** (Aczone) is a sulfone with antibacterial and anti-inflammatory activity, effective for both inflammatory and noninflammatory acne. It may benefit patients sensitive or intolerant to standard treatments and can be used in sulfonamide-allergic individuals. **Dapsone** 5% gel is applied twice daily; 7.5% gel is applied once daily. Combination with topical retinoids may be appropriate for comedonal lesions. **Dapsone** 5% gel has also been combined with **adapalene** or benzoyl peroxide.

Oral Antibacterials

- Oral antibiotics are reserved for moderate-to-severe inflammatory acne.
- **Tetracyclines** (**minocycline**, **doxycycline**) are first-line due to antibacterial and anti-inflammatory effects.
- Macrolides (**erythromycin**, **azithromycin**) and **trimethoprim/sulfamethoxazole** are acceptable alternatives. Due to resistance,

erythromycin should be limited to patients who cannot take **tetracyclines** (eg, pregnant women, children under 8).

- **Ciprofloxacin** and **trimethoprim** alone may be used when other antibiotics are unsuitable or ineffective.
- **Sarecycline** (Seysara), a narrow-spectrum **tetracycline** with anti-inflammatory action, is approved for inflammatory lesions of non-nodular moderate-to-severe acne in patients ≥ 9 years.
- Oral antibiotics should be started with combination therapy including retinoids. In many cases, antibiotics can be stopped after 3–6 months.
- The incidence of significant adverse effects with oral antibiotics is low. Vaginal candidiasis can occur with all oral antibiotics. Minocycline may cause pigment deposition in skin, mucous membranes, and teeth and may lead to dose-related dizziness, urticaria, hypersensitivity syndrome, autoimmune hepatitis, lupus-like syndrome, and serum sickness-like reactions. **Doxycycline** is a photosensitizer, especially at higher doses.
- Antibiotic selection should be guided by side effect profile, resistance, cost, and consensus guidelines.

Intralesional Corticosteroids

Intralesional **triamcinolone acetonide** is effective for large inflammatory nodules, providing rapid improvement and pain relief, though it may cause local skin atrophy.

Hormonal Agents

- Oral contraceptives containing estrogen may help treat acne in some women due to antiandrogenic effects. FDA-approved options include **norgestimate + ethinyl estradiol** and **norethindrone acetate + ethinyl estradiol**; other estrogen-containing products may also be effective. They can be used alone or with other acne therapies.
- **Spironolactone**, an antiandrogen, is effective for acne in select women. The usual dose is 50–100 mg daily. It may cause hyperkalemia, especially at higher doses or in those with cardiac or renal issues. It is not FDA approved for acne and should not be used in males.
- **Clascoterone** 1% cream (Winlevi) is an androgen receptor inhibitor approved for acne in males and females ≥ 12 years. Applied twice daily, common side effects include erythema, edema, and dryness/scaling.
- **Oral corticosteroids**, used in high doses short-term, may benefit severe inflammatory acne. Low-dose **prednisone** (5–15 mg daily), alone or with high-estrogen contraceptives, has shown efficacy for acne and seborrhea. Long-term side effects limit its use as primary therapy.

Isotretinoin

- **Isotretinoin**, a vitamin A metabolite, reduces sebum production, inhibits *C. acnes*, and decreases inflammation. It is approved for severe recalcitrant nodular acne in nonpregnant patients aged 12 and older with multiple inflammatory nodules ≥ 5 mm. It is also used for moderate acne that is treatment-resistant, relapses after oral antibiotics, or causes scarring or significant psychosocial distress. **Isotretinoin** is the only acne treatment that induces prolonged remission.
 - ✓ The approved **isotretinoin** dose is 0.5–2 mg/kg/day, typically over a 20-week course. Absorption improves when taken with food.
 - ✓ Initial flares can be reduced by starting at ≤ 0.5 mg/kg/day, then increasing to 1 mg/kg/day after the first month as tolerated. The target cumulative dose is 120–150 mg/kg.
 - ✓ Side effects commonly affect mucocutaneous, musculoskeletal, and ophthalmic systems, along with headaches and central nervous system effects. Most effects, like cheilitis and dryness of the nose, eyes, and mouth, are temporary and resolve after stopping treatment.
 - ✓ Laboratory abnormalities include hypertriglyceridemia, transaminitis, thrombocytopenia, and leukopenia, though these rarely cause clinical issues. A Delphi consensus in 2022 recommended checking only alanine aminotransferase and triglycerides at treatment initiation and peak dose. Mood disorders, including depression and suicidal ideation, have been reported, but no causal link to **isotretinoin** is established. These conditions also occur in severe acne without treatment.

✓ Due to teratogenicity, two forms of contraception must begin 1 month before treatment in females of childbearing potential, continue during therapy, and for 4 months after stopping. All patients must enroll in the iPLEDGE program, which requires pregnancy tests and verification by prescribers and pharmacists of adherence to safety protocols.

EVALUATION OF THERAPEUTIC OUTCOMES

- Provide acne patients with a monitoring framework outlining specific parameters and frequency. Have them track treatment response in a diary. Follow up within 2–3 weeks of starting therapy, then every 4–8 weeks.
- Adherence is key to treatment success. Lesion counts should drop by 10%–15% in 4–8 weeks and over 50% in 2–4 months. Inflammatory lesions typically resolve in a few weeks and comedones in 3–4 months. If anxiety or depression is present, improvement should occur within 2–4 months.
- Long-term goals include stable severity, extended acne-free periods, and no new scarring or pigmentation.
- Monitor regularly for adverse effects and adjust with dose changes, alternative treatments, prevention strategies, or discontinuation as needed.

See [Chapter 123](#), *Acne Vulgaris*, authored by Debra Sibbald and Cathryn Sibbald, for a more detailed discussion of this topic.